REMARKS

Claims 1-6 and 9-34 are pending. Claims 4, 7-13, and 18-34 have been canceled.

INTERVIEW SUMMARY

Applicant would like to thank Examiner Kolker for his comments during the phone call of May 21, 2007 to discuss the Office Action mailed March 2, 2007 as well as proposed arguments and possible amendments to the claims.

Regarding the substance of the Office Action, the rejections under 35 U.S.C. § 112, first paragraph were discussed. Applicants raised the issue that all embodiments need not be operable in order to be enabled. Examiner Kolker indicated that Applicants were welcome to make such arguments in their Response and he would consider the arguments, however no agreement was made as to whether such arguments would satisfy 35 U.S.C. § 112, first paragraph. Applicants also raised the possibility of filing a declaration, which Applicants now attach to this Amendment and Response and discuss below.

Applicants also discussed the possibility of making amendments to the claims to avoid further arguments and to expedite examination on the merits. Examiner Kolker agreed to view any proposed amendments, however Applicants chose not to amend the claims and to present the arguments below.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

1. Claims 1-4, 6, and 14-17 were rejected under 35 U.S.C. § 112, first paragraph, as not being enabled. Applicants respectfully traverse this rejection.

Any analysis of whether a particular claim is enabled by the disclosure in an application requires a determination of whether that disclosure, when filed, contained sufficient information

regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention. The test of enablement is whether one skilled in the art could make or use the claimed invention from the disclosures in the patent coupled with information known in the art without undue experimentation. *United States v. Telectronics, Inc.*, 857 F.2d 778, 8 USPQ2d 1217 (Fed. Cir. 1988); *In re Stephens*, 529 F.2d 1343, 199 USPQ 659 (CCPA 1976). A patent need not teach, and preferably omits, what is well known in the art. *Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524, 3 USPQ2d 1737 (Fed. Cir. 1987). Determining enablement is a question of law based on underlying factual findings. *In re Vaeck*, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991); *Atlas Powder Co. v. E.I. duPont de Nemours & Co.*, 750 F.2d 1569, 224 USPQ 409 (Fed. Cir. 1984).

Applicants first note that claim 4 has been canceled and therefore submit that the rejection of claim 4 is moot.

With respect to the remaining claims the Office Action on page 3, lines 17-18, alleges that claims 1-4, 6-8, and 14-17, while being enabled for the polypeptide comprising SEQ ID NO:5, does not provide enablement for the broad genus of polypeptides as claimed in pending claim 1.

The Examiner appears to base his rejection on the notion that the polypeptide recited in claim 1 is broad and "encompasses a very large number of possible protein sequences that the specification does not disclose how to use." (See Office Action page 3, lines 15-17). The Office Action further alleges on page 3, lines 17-26, that claim 1 encompasses proteins that do not enhance binding or degredation of LDL and VLDL as provided in dependent claims 14 and 15. Examiner Kolker during the telephone interview of May 21, 2007, further alleged that the claims

were not enabled based on a similar premise that there could be proteins that are encompassed by claim 1 that are inoperable or useless.

Examiner's Burden

Applicants respectfully submit that an invention need be only minimally operable and that the Patent Office is burdened with establishing that the claimed invention is inoperable. The rejection appears to be based on the assumption that some of the claimed synthetic apolipoprotein-E mimicking polypeptide sequences would be useless based on an unsupported allegation that some of the polypeptide sequences may not enhance binding or degredation of LDL and VLDL and therefore would not be operative in any method. In this regard, the rejection theorizes, without support, that simply because the claimed polypeptide sequences are broadly drawn and allow for a limited variation in certain positions of the polypeptide sequence, this would prevent the polypeptides from having any use described within the specification.

Applicants first note that the rejection has failed to meet the burden to establish that the claimed polypeptides would be inoperable. Mere unsupported theory is not enough. In re Gaubert, 524 F.2d 1222, 1224 (CCPA 1975). Neither the previous, nor the current rejection has presented any evidence that the claimed polypeptids would be unable to enhance binding of low-density lipoprotein (LDL) or very low density lipoprotein (VLDL) to a cell and so has not established a prima facie case of lack of enablement.

All Embodiments Need Not Be Operable

Applicants also respectfully point out that the possible inoperability of some embodiments which can be construed to be encompassed by a claim is not a bar to patentability. It is not a function of the claims to exclude every possible inoperable embodiment and

Applicants are not required to do so.[1] As such, Applicants respectfully submit that not all embodiments need be operable in order for a claim to be enabled.

Applicants also submit, that the majority, if not all, of the embodiments are operable and that one of skill n the art would understand such without resorting to undue experimentation. The Office Action appears to have concern that changing one or two residues can result in changing a large degree of the structure of a protein (See Office Action page 3, line 33 –page 4, line 1). Applicants note that claim 1 currently recites "wherein the polypeptide is capable of forming an amphipathic α helical structure". As such, the polypeptides recited in claim 1 have a finite structure and if a change in the sequences did result in a change in structure, namely that of a structure other than an amphipathic α helical structure, such peptides would fall outside the claimed invention. As such, Applicants submit that such an argument is moot.

The Office Action also alleges on page 4, lines 1-5) that random protein mutations could result in inactive proteins. The Office Action further alleges that the mere fact that the claimed polypeptides form amphipathic alpha helices does not limit them to those proteins which the specification teaches the artisan how to use (See Office Action page 4, lines 16-18). The Office Action cites Bechinger et al. and Kandel for allegedly supporting that proteins comprising such helices are found in different locations of proteins as well as in transcription factors. While this may be true, neither Bechinger et al. nor Kandel speak to the particular apolipoprotein-E

[1]See *In re Anderson*, 471 F.2d 1237, 1242 (CCPA 1973), ("[I]t is always possible to put something into a combination to render it inoperative. It is not a function of the claims to *exclude* all such matters but to point out what the combination is."); *Ex parte Cole*, 223 USPQ 94, 95-96 (PTO Bd. App. 1983) ("Claims are addressed to the person of average skill in the particular art. Compliance with 112 must be adjudged from that perspective, not in a vacuum. It is always possible to theorize some combination of circumstances which would render a claimed composition or method inoperative, but the art skilled would assuredly not choose such a combination."); *Horton v. Stevens*, 7 USPQ2d 1245, 1247 (Bd. Pat. App. & Int'f 1988) ("The mere fact that a claim embraces undisclosed or inoperative species or embodiments does not necessarily render it unduly broad."); and *Ex parte Breuer*, 1 USPQ2d 1906 at 1906 (Bd. Pat. App. & Int'f 1986) ("The issue is not whether the examiner can conjure up a substituent group...which does not exist. A person having ordinary skill in the art would readily appreciate that compounds containing such substituent group[s] do not exist....'[N]obody will use them...and the claims do not cover them'.")

mimicking peptides currently claimed. As discussed in Applicants' previous Response, although claim 1 allows for a number of permutations within the core sequence, the number of permutations is not only limited by the number of possible permutations, but the amino acid substitutions are restricted to the specific locations and amino acid residues that can be substituted.

Furthermore, no matter how many permutations are possible, each and every polypeptide within the genus is capable of forming the same structure, namely an amphipathic α helical structure. A critical error in the present rejection is the apparent view that the claims require only formation of an amphipathic α helical structure. It is not just the amphipathic α helical structure, but it is also the amino acid chemistry that matters. Applicants are claiming a subset of amino acid sequences that can form an amphipathic α helix and the claims are limited to those peptides that would such a pattern of amino acids.

As such, Applicants submit that it is very important to note that it is not only the amphipathic helical structure that confers the desired utility of the claimed polypeptides, but it is the amphipathic helical structure that contains at least one Arg residue on the polar face of the amphipathic helix that allows the claimed polypeptides to associate with atherogenic LDL and VLDL and remnant lipoproteins to enhance their hepatic uptake and degradation. (See Example 1 and paragraphs 5 and 6 of the declaration of Dr. Gattadahalli M. Anantharamaiah, Ph.D.). In other words, it has been demonstrated that a variety of different apolipoprotein E mimicking peptides are capable of decreasing plasma cholesterol levels, as most of the sequences given above. It has also been shown that the ability of the peptides to form an amphipathic α-helical structure by increasing the width of the polar face either by substituting Lys with Arg or by dimethylation of lysine will enhance binding of low-density lipoprotein (LDL) or very low

density lipoprotein (VLDL) to a cell. Disruption of this structure removes the ability to decrease plasma cholesterol levels. Dr. Anantharamaiah, a pioneer and expert in this field, states that based on his experience and the evidence discussed above, "I conclude that the evidence indicates that so long as the peptides mimic apolipoprotein E peptides, namely by sharing a similar sequence and being able to form an amphipathic alpha helical structure with a widened polar face either by substituting Lys with Arg or by dimethylation of lysine, that the peptide will be able to decrease plasma cholesterol levels." (See paragraph 7 of the declaration of Dr. Gattadahalli M. Anantharamaiah, Ph.D.)

As such, Applicants submit that the skilled artisan would not have to resort to a large degree of experimentation to determine how to use the claimed polypeptides as the specification establishes the function and further provides a road map of how the experiments were performed such that one of skill in the art could easily follow.

In addition, with respect to the Advisory Action of August 13, 2007, Applicants submit that because a Request for Reconsideration has been filed with the current Amendment, 37 C.F.R. 1.116 no longer applies and therefore there need not be a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. In other words, since the current Amendment is not being submitted after a final rejection or other final action, 37 C.F.R. 1.116 is not applicable. As such, Applicants respectfully request consideration of the attached Declaration of Dr. Anantharamaiah as evidence of patentability.

For all the reasons above, Applicants respectfully submit that the specification not only teaches how to use the polypeptides recited in claim 1, but the specification provides how to use the claimed polypeptides. Applicants further submit that due to the extensive teachings cited above, as well as the attached declaration of Dr. Gattadahalli M. Anantharamaiah, Ph.D. it would

not require undue experimentation on the part of a skilled artisan to make and use the claimed invention commensurate in scope to the claims. For at least these reasons, Applicants submit that claims 1-4, 6, and 14-17 are fully enabled. As such, Applicants respectfully request withdrawal of this rejection.

A Credit Card payment in the amount of $680.00, $285.00 representing the difference between the Two month Extension of time fee previously paid for on July 31, 2007 and a three month extension of time pursuant to 37 C.F.R. §1.17(a)(3) and $395.00 for the fee for a small entity under 37 C.F.R. §1.17(e); a Request for Extension of Time; a declaration of Gattadahalli M. Anantharamiah under 37 C.F.R. § 1.132; and a Request for Continued Examination are enclosed. This amount is believed to be correct; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

NEEDLE & ROSENBERG, P.C.

Scott D. Marty
Registration No. 53,277

NEEDLE & ROSENBERG, P.C.
Customer Number 23859
(678) 420-9300
(678) 420-9301 (fax)

CERTIFICATE OF EFS-WEB TRANSMISSION UNDER 37 C.F.R. § 1.8

I hereby certify that this correspondence, including any items indicated as attached or included, is being transmitted by EFS-WEB on the date indicated below.

Scott D. Marty, Ph.D.

9-4-07

Date